HFD-613

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-790/S-007
NDA 20-215/S-008

JAN 1 3 1999

Schwarz Pharma, Inc.
Attention: Ms. Donna K. Multhauf
P.O. Box 2038
Milwaukee, WI 53201

Dear Ms. Multhauf:

Please refer to your supplemental new drug applications dated November 18 and 19, 1998, received November 19 and 20, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Monoket (isosorbide mononitrate) Tablets (NDA 20-215) and Dilatrate (isosorbide dinitrate) Sustained Release Capsules (NDA 19-790), respectively.

These supplemental new drug applications provide for final printed labeling revised by adding the following in bold print as the first paragraph of the WARNINGS section of the labeling:

> **Amplification of the vasodilatory effects of Monoket/Dilatrate by sildenafil can result in severe hypotension. The time course and dose dependence of this interaction has not been studied. Appropriate supportive care has not been studied, but it seems reasonable to treat this as a nitrate overdose, with elevation of the extremities and with central volume expansion.**

We have completed the review of these supplemental applications and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the final printed labeling included in your November 18 and 19, 1998 submissions. Accordingly, these supplemental applications are approved effective on the date of this letter.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Mr. Gary Buehler
Regulatory Health Project Manager
(301) 594-5332

Sincerely yours,

Raymond J. Lipicky, M.D.
Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research